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# Asymmetric lithium(I) and copper(II) alkoxy-*N*-heterocyclic carbene complexes; crystallographic characterisation and Lewis acid catalysis†

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**A one-pot synthesis of a wide range of bidentate, alkoxide-*N*-heterocyclic carbene ligands provides new lithium alkoxy-carbenes and a range of covalently bound organometallic Cu(II) carbene complexes, which are catalytically active, in some cases enantioselectively, for conjugate addition reactions.**

Nucleophilic *N*,*N′*-disubstituted imidazol-2-ylidenes, or *N*-heterocyclic carbenes (NHCs), are strong σ-Lewis bases. As such they have already found use as LAC (ligand accelerated catalysis) additives that can improve the activity of Lewis acid metal catalyst systems. For example, the ring opening of *meso*-epoxides by triethylaluminium is catalysed by 5 mol% of [:C{(NAr)CH$_2$}$_2$], or the complex [AlEt$_3$(:C{(NAr)CH$_2$}$_2$)] (Ar = 2,6-Pr$^i_2$–C$_6$H$_3$); the latter is a superior catalyst (the imidazolinium-catalysed reaction also generates other by-products).[1] The copper-catalysed conjugate addition (Michael addition) of diethyl zinc to cyclohexenone has also been improved by the addition of an *in situ* generated NHC, [:C{(NR)CH}$_2$] (R = mesityl), or the silver carbene [Ag(:C{(N-Me)CHBu$^t$}$_2$)];[2] the latter is assumed to form a copper carbene catalyst *in situ*. Despite much recent interest in NHC-derived catalysts, there are still few applications in asymmetric synthesis.[3]

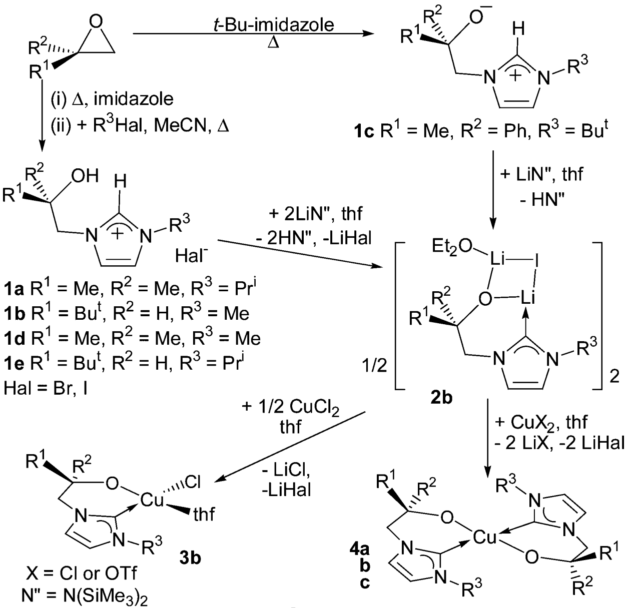
We have been studying polydentate ligands that combine the NHC group with an anionic functional group, to stabilise higher oxidation state, and Lewis acidic metal catalysts.[4] There are many Cu(I) complexes of neutral, soft NHCs.[5] Despite the use of *in situ* generated mixtures of NHCs and Cu(II) salts in Lewis acid catalysed reactions such as conjugate addition, only one isolated divalent copper-NHC complex has been reported, stabilised by the use of an encapsulating tris(NHC) ligand.[6] It is proposed that a high oxidation state Cu(III)-enolate intermediate forms in copper-catalysed conjugate addition reactions, so an NHC ligand that stabilises higher oxidation state complexes should provide a LAC effect in such a catalysed reaction.

Herein, we report one-pot syntheses of asymmetric alkoxy-functionalised NHCs that are capable of stabilising Cu(II) carbene complexes, the synthesis and catalytic reactivity of lithium and copper complexes, and the first crystallographically characterised copper(II) carbene.

The reaction of 2-*tert*-butyl epoxide with imidazole in acetonitrile, then with isopropyl iodide yields the imidazolium iodide [HOCMe$_2$CH$_2$(1-HC{NCHCHNPr$^i$})]I [H$_2$LI] **1a**, in excellent yield (see ESI†). This reaction is general; Scheme 1. Sterically more demanding *N*-substituents can be incorporated by the use of preformed alkyl imidazoles; an alternative route forms, for example, the zwitterionic **1c** [HOCMePhCH$_2$(1-HC{NCHCHNBu$^t$})] [HL]. Single crystal X-ray diffraction studies of ligands **1a**, **1c**·HCl, and **1d** show the protonated alcohol and imidazolium groups of the proligand (see ESI†)‡.

Deprotonation of **1** with two equivalents of lithium *n*-butyl or LiHMDS (one for **1c**) affords the colourless crystalline lithium alkoxide-carbenes [LiOCR$^1$R$^2$CH$_2$(1-C{NCHCHNR$^3$})], LiL, **2**, recrystallised with an equivalent of the lithium halide by-product (for iodide), in excellent yields, Scheme 1. Single crystals of **2b**·LiI were grown from a diethyl ether solution, Fig. 1.§ Although grown from a racemate, the crystal is homochiral. The structure is a dimer of LiL, with stoichiometric incorporated LiI, which forms a tetrameric butterfly of lithium cations. The Li–C$_{carbene}$ distance of 2.135 Å is the shortest yet reported.[7] Despite this, the Li–NHC fragment is distorted; the NHC–C$_{carbene}$–Li angle is 152.3° rather than 180°. The two iodides each cap a Li$_3$ unit, but are not close enough to suggest any I···I bond (4.14 Å).

The lithium salts **2** react with half or one equivalent of copper(II) chloride or copper(II) triflate to afford mono- or bis-substituted Cu(II) alkoxy-carbene complexes, isolated as lithium iodide adducts, Scheme 1, [Cu{OCR$^1$R$^2$CH$_2$(1-C{NCHCHNR$^3$})}Cl(thf)(LiI)] **3** and [Cu{OCR$^1$R$^2$CH$_2$(1-C{NCHCHNR$^3$})}$_2$(LiI)$_2$] **4** respectively, after recrystallisation from toluene or thf.¶ The paramagnetism of the complexes precludes $^{13}$C NMR spectroscopic identification of the carbene; unsurprisingly we were unable to detect a hyperfine coupling to the carbene by X-band EPR.† Complexes **4** are sufficiently air stable to show the parent ion in electrospray MS. This makes their potential for use as homogeneous Lewis acid catalysts most promising.[8]



**Scheme 1**

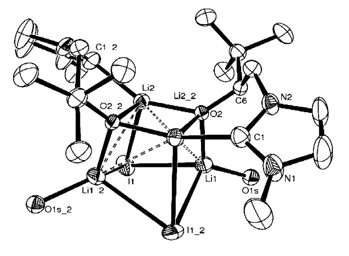


**Fig. 1** Thermal ellipsoid drawing of **2b**. H and coordinated solvent C omitted. Distances (Å) and angles (°): Li(1)–O(2) 1.888(6), Li(2)–O(2) 1.893(5), Li(1)–Li(2) 2.831(8), Li(1)–I(1) 2.838(6), Li(2)–I(1) 2.904(5), O(2)–C(6) 1.404(4), N(1)–C(1) 1.358(4), O(2)–Li(2)–O(2)_2, 98.2(2).

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† Electronic supplementary information (ESI) available: full synthetic and structural details. See http://www.rsc.org/suppdata/cc/b4/b404614e/

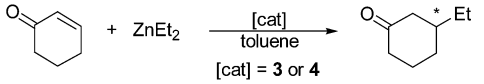
The Cu(II)–carbene fragment is interesting in its own right since it is implicated in so many copper catalysed carbene transfer reactions, but usually is too reactive to isolate and study.[9] Despite growing a range of crystals of **3** and **4** that appeared optically to be suitable for single crystal X-ray diffraction, we have been unable to obtain diffraction patterns from any. However, careful oxidation of $[Cu\{OC(Ph)(CH_2\{1\text{-}C[NCHCHNBu^t]\})_2\}]_2$ ($[CuL^o]_2$) previously made in our laboratory,[4] afforded an orange, highly crystalline, tetrametallic complex in very low yield, 5%, characterised as $[\{(\mu\text{-}O)[CuClL^o]_2\}_2]$ **5**, Fig. 2.‖

To the best of our knowledge there is only one other crystallographically characterised organometallic Cu(II) complex; the *N*-confused porphyrin complex $[Cu^{II}\{calix[4]phyrin\}]$ has a 2.007(4) Å Cu–C distance, the average Cu(II)–C distance in **5** is 1.99(3) Å. The Cu centres are slightly distorted square planes with the alkoxide O atom displaced out of the plane by 0.102 Å.

As well as being rare examples of organometallic Cu(II),[10] these are the first complexes that tether the NHC group to the copper(II) centre by an anionic group, providing an alternative source of stereocontrol in **3** or **4**. NHCs are usually rendered chiral by incorporation of a chiral hydrocarbyl *N*-substituent *e.g.* $[:C\{(NCH(Ph)Me)CH\}_2]$, or by $C_2$ symmetrical 1,2-dialkylation of the backbone of the saturated NHC analogue, *e.g.* $[:C\{(NR)CHBu^t\}_2]$.

The catalysis of conjugate addition to cyclohexenone, eqn. (1), by **3** and **4** has been studied. Complex (R)–**2b** was used to make enantiomerically pure **3b**. All the complexes tested show rapid and high-yielding catalysis of the substrate, as would be predicted from the bound NHC donor group, Table 1.

The most efficient catalyst is the *N*-methylated *t*-butoxide **3b**. This NHC group is the least sterically encumbered, but makes the poorest NHC donor. There are no reports of the use of copper alkoxides as catalysts for conjugate addition reactions, but it is possible that the alkoxide also contributes to the activity of this catalyst. The homochiral complex gave an ee of 51%. This represents good (3 : 1) selectivity, particularly at this relatively high temperature and short reaction time.



(1)

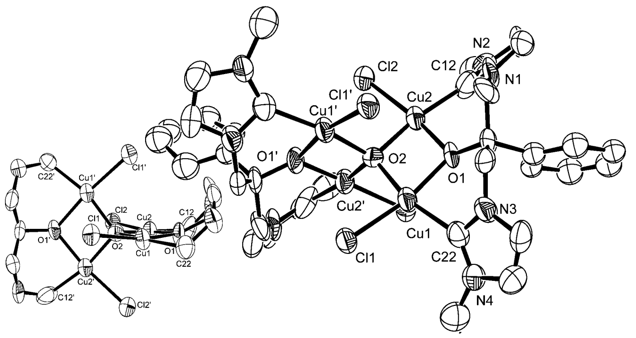


**Fig. 2** Thermal ellipsoid drawing of **5**. Distances (Å) and angles (°): Cu1–C22 2.008(13), Cu1–O1 1.979(7), Cu1–O2 1.958(6), Cu2–C12 1.971(15), N1–C12–N2 105.4(14), N1–C12 1.38(2); $Cu_4$ core inset.

**Table 1** Results of copper catalysed conjugate addition[a]

| Complex | Catalyst conc. (mol %) | Time/h | Conversion (%) | ee (%) |
|---|---|---|---|---|
| **3b** | 5 | 2 | 100 | 51(*S*) |
| **3c** | 5 | 2 | 78 | — |
| **4a** | 5 | 2 | 72 | — |
| **4b** | 5 | 2 | 98 | — |
| **4c** | 5 | 2 | 60 | — |

[a] All reactions at −30 °C under purified $N_2$ atmosphere.

A recent study of catalysts made from copper(II) salts with added chiral monodentate NHC ligands gave ees of up to 39% at −20 °C with $[:C\{(NCH(Ph)Me)CH\}_2]$, (but with a yield of 60%), with improved enantioselectivities at −78 °C over 16 h (to 69% ee), or with a different test substrate ketone.[11]

In summary, a range of new anionic, heterobidentate ligands that combine the strong σ-donor *N*-heterocyclic carbene with an alkoxide, and the first characterised lithium salts of a bidentate NHC ligand are easily made. Chiral complexes of rare divalent copper organometallics have been isolated, these catalyse conjugate addition reactions. The first crystal structure of a non-macrocyclic organometallic copper(II) complex has also been presented. The insight into the Cu(II)–NHC moiety should aid in future catalyst, or LAC additive, design.

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## Notes and references

‡ Crystallographic data for all complexes are deposited with the CCDC: CCDC 235713–235718. See http://www.rsc.org/suppdata/cc/b4/b404614e/ for crystallographic data in .cif or other electronic format.

§ **2b** C28 H54 I2 Li4 N4 O4 $M_r$ = 792.31, monoclinic, $a$ = 12.880(2), $b$ = 15.655(2) $c$ = 19.034(2) Å, $\beta$ = 93.239(2)°, $U$ 3831.8 Å$^3$, $T$ = 150 K, space group $C2/c$, $Z$ = 4, $d_c$ = 1.373 Mg m$^{-3}$, $\mu$(Mo–Kα) = 1.674 mm$^{-1}$ 11901 unique reflections ($R_{int}$ = 0. 031) used in all calculations. Final $R_1$ [4326 reflections with $F > 4\sigma(F)$] = 0.0362 and $wR$(all $F^2$) was 0.0854.

¶ **3b**: pale green solid, yield 63%. **4a**: purple solid, yield 69%. **4b**: purple solid, yield 76%. Anal. calcd. (found) for $C_{20}H_{34}CuN_4O_2{\cdot}2.5C_7H_8{\cdot}2LiI$: C, 48.74 (49.05); H, 5.89 (5.27); N, 6.06(6.74).

‖ **5**: C48.4 H65.6 Cl4 Cu4 N8 O3.6 $M_r$ = 1215.46, tetragonal, $a = b$ = 14.763(3), $c$ = 27.053(6) Å, $U$ 5896(4) Å$^3$, $T$ = 150(2) K, space group $P4_12_12$, $Z$ = 4, $d_c$ 1.369 Mg m$^{-3}$, $\mu$(Mo–Kα) = 1.649 mm$^{-1}$ 7023 unique reflections ($R_{int}$ = 0.189) used in all calculations. Final $R_1$ [5208 reflections with $F > 4\sigma(F)$] = 0.0645 and $wR$(all $F^2$) was 0.214.

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